

CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY  
DEPARTMENT OF PESTICIDE REGULATION  
MEDICAL TOXICOLOGY BRANCH  
SUMMARY OF TOXICOLOGY DATA  
CHROMIC ACID\*

Chemical Code # 001188, Tolerance # 51007  
SB 950 # 589  
November 30, 2000

I. DATA GAP STATUS

Chronic, rat:	Data gap, no adverse effect indicated.
Oncogenicity, rat:	Data gap, inadequate study, possible adverse effect indicated.
Chronic toxicity, dog:	Data gap, study inadequate, no adverse effect indicated.
Oncogenicity, mouse:	Data gap, no study on file.
Reproduction, rat:	Data gap, no study on file.
Teratology, mouse:	No data gap, possible adverse effect
Teratology, rabbit:	Data gap, inadequate study, possible adverse effect indicated.
Gene mutation:	No data gap, possible adverse effect.
Chromosome effects:	No data gap, possible adverse effect.
DNA damage:	No data gap, possible adverse effect.
Neurotoxicity:	Not required at this time

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Toxicology one-liners are attached.

All record numbers through 133223 were examined.

\*\* indicates an acceptable study.

**Bold face** indicates a possible adverse effect.

File name: T001130.

Original by: Kishiyama & Silva, 11/30/00

\* Chromic acid category includes aqueous solutions of hexavalent chromium compounds sodium dichromate [ $\text{Na}_2\text{Cr}_2\text{O}_7$ ], sodium chromate,  $\text{Na}_2\text{CrO}_4$ , potassium dichromate (DPN# 50548; [ $\text{K}_2\text{Cr}_2\text{O}_7$ ]) and chromium trioxide [ $\text{CrO}_3$ ].

Note: Hexavalent chromium was listed as a carcinogen under California's Proposition 65 in 1987.

## II. TOXICOLOGY ONE-LINERS AND CONCLUSIONS

These pages contain summaries only. Individual worksheets may contain additional effects.

### CHRONIC TOXICITY, RAT

001 045396 "Chronic Toxicity Studies: II. Hexavalent and Trivalent Chromium Administered in The Drinking Water to Rats," (MacKenzie, R.D., Byerrum, R.U., Decker, C.F., Hoppert, C.A., Langham, R.F.; Archives of Industrial Health, 18:232-234, 1958). **Experiment #1:** Potassium chromate ( $\text{K}_2\text{CrO}_4$ ) was administered in the drinking water at 0, 0.45, 2.2, 4.5, 7.7 and 11 ppm (Cr) to Sprague-Dawley rats (8/sex/dose). Results showed chromium accumulation was greatest at  $\geq 5$  ppm, with spleen being significantly greater than liver, kidney and bone. **Experiment #2:** Chromium was used in drinking water as CrVI ( $\text{K}_2\text{CrO}_4$ ) and as CrIII ( $\text{CrCl}_3$ ) at 25 ppm in (9/sex/group) for one year. Chromium concentrations in tissues were approximately 9 times higher in Cr VI ( $\text{K}_2\text{CrO}_4$ ) than in CrIII ( $\text{CrCl}_3$ ). Water intake was decreased in animals receiving CrVI, since females drank 77% and males drank 84% as much as the controls. No adverse effect indicated. No toxic symptoms were reported in either experiment. No microscopic changes were reported in Experiment #1. These data are supplemental. (Kishiyama & Silva, 10/11/00).

### CHRONIC TOXICITY, DOG

001 045395 "Chronic Toxicity Studies: III. Chronic Toxicity of Cadmium and Chromium in Dogs," (Anwar, R.A., Langham, R.F., Hoppert, C.A., Alfredson, B.V., Byerrum, R.U.; The Departments of Chemistry, Pathology and Physiology and Pharmacology, Michigan State University, MI; 5/3/61; Published in Archives of Environmental Health, 3: 456-460, 1961). Potassium chromate ( $\text{K}_2\text{CrO}_4$ ) was administered in the drinking water to female dogs for 4 years at 0 (1 dog, breed not mentioned), 0.45 (2 dogs: German Shepherd & Poodle), 2.25 (2 dogs: German Shepherd & poodle), 4.5 (1 German Shepherd), 6.75 (2 Beagles) and 11.2 ppm (2 Beagles). Dogs receiving chromium as chromate in drinking water showed accumulation of Cr in liver, kidney and spleen (independent of concentration of Cr in water). Accumulation was greatest in the liver. No other significant treatment-related findings were observed after 4 years of treatment in drinking water. Water intake was not reported. No adverse effect indicated. These data are supplemental. (Kishiyama & Silva, 10/10/00).

### ONCOGENICITY, RAT

**011 132934** "Carcinogenicity of Sodium Dichromate and Chromium (VI/III) Oxide Aerosol Inhaled by Male Wistar Rats," (Glaser, U., Hochrainer, D., Kloppel, H., Oldiges, H.; Published in Toxicology, 42:219-232, 1986). Sodium dichromate ( $\text{Na}_2\text{Cr}_2\text{O}_7$ ) at 0, 25, 50 or 100  $\mu\text{g}/\text{m}^3$  and chromium oxide mixture ( $\text{Cr}_5\text{O}_{12}$ ; CrVI/CrIII, 3:2 mixture; concentration of Cr = 100  $\mu\text{g}/\text{m}^3$ ) were administered in an aerosol to male

Wistar TNO-W74 rats (20/dose; 40 rats for control level) for 18 months (22-23 hours/day; 7 days/week). All rats on test were held for an additional year without exposure to test compounds. More than 90% of rats survived 2 years (termination mortality = 42.5%, 35%, 45%, 25% for  $\text{Na}_2\text{Cr}_2\text{O}_7$  & 50% for  $\text{Cr}_5\text{O}_{12}$  groups, respectively).  $\text{Cr}_5\text{O}_{12}$ -treated rats showed elevated white and RBC counts and serum cholesterol, with decreased serum immunoglobulin levels and increased lung histopathology (due to increased Cr burden). At termination, lung Cr retention was about 10-times higher for the rats exposed to  $\text{Cr}_5\text{O}_{12}$  versus  $\text{Na}_2\text{Cr}_2\text{O}_7$  at an aerosol concentration of  $100 \text{ ug/m}^3$ , while the kidney Cr retention was measured to be virtually equal between groups. Three primary lung tumors (2 adenomas & 1 adenocarcinoma) and 1 malignant tumor of the pharynx were observed at  $100 \text{ ug/m}^3$   $\text{Na}_2\text{Cr}_2\text{O}_7$ . One primary adenoma was observed in the  $\text{Cr}_5\text{O}_{12}$ -exposed rats at  $100 \text{ ug/m}^3$ . **Possible adverse effect indicated.** These data are supplemental. (Kishiyama & Silva, 10/19/00).

**001 045397** "Experimental Studies in Metal Cancerigenesis: X. Cancerigenic Effects of Chromite Ore Roast Deposited in the Muscle Tissue and Pleural Cavity of Rats," (Hueper, W.C.; Archives of Industrial Health, 18:284-291, 1958). Chromium cubes (prepared by mixing 25 mg chromite ore roast with 75 mg sheep fat) were implanted into the pleural cavity of Bethesda black male rats (25/dose) and into the muscle tissues of the right thigh of females (31/dose). Controls were: intramuscular and intrapleural sheep fat implants in females (15 rats/location). Rats were sacrificed after 2 years of treatment. Mortality was high, primarily in males with an intrapleural chromium cube (23/25 by 19-21 months). Females with intramuscular chromium cubes had 18/31 deaths by 19-21 months. Control mortality was also high (lung implant: 12/15; intramuscle: 12/15 at 19-21 months). Chronic inflammatory pathology was observed, primarily in lung. **Two/25 males developed squamous-cell carcinomas/sarcomas of the lung and 3/31 females developed fibrosarcomas of the thigh muscle. Possible adverse effect.** These data are supplemental. (Kishiyama & Silva, 10/11/00).

**013 132946** "Carcinogenicity and Mutagenicity of Chromium Compounds," (Levy, L.S., Venitt, S.; The Institute of Occupational Health, University of Birmingham, Birmingham, UK and Institute of Cancer Research, Surrey, UK; Published in Carcinogenesis 7:831-936, 1986). Hexavalent ( $\text{Cr}[\text{VI}]$ -genotoxic) and trivalent ( $\text{Cr}[\text{III}]$ -nongenotoxic) chromium-containing compounds were administered to Porton-Wistar rats (48 M & 52 F/group) and were compared for incidence of squamous metaplasia in bronchial epithelium. 20-Methylcholanthrene was used as a positive control. A stainless steel pellet loaded with 2 mg test material (suspended in cholesterol) was inserted in the left bronchus via tracheotomy (under anaesthesia). After two-years,  $\text{CrVI}$  compounds showed and an increase in squamous metaplasia (preneoplasia). The incidence increased as solubility decreased (low solubility = zinc potassium chromate [ $\text{K}_2\text{CrO}_4 \cdot 3\text{ZnCrO}_4 \cdot \text{Zn}(\text{OH})_2$ ] & calcium chromate [ $\text{CaCrO}_4$ ]; higher solubility = chromium trioxide, sodium dichromate & sodium chromate). **Possible adverse effect:**  $\text{CaCrO}_4$  and  $\text{K}_2\text{CrO}_4 \cdot 3\text{ZnCrO}_4 \cdot \text{Zn}(\text{OH})_2$  induced lung carcinoma in the rats. Because of the metaplasia (considered preneoplastic), the  $\text{CrVI}$  compounds were considered as "pro-carcinogen." These data are supplemental. (Kishiyama & Silva, 10/10/00).

001 058465 "Absence of Toxic and Carcinogenic Effects after Administration of High doses of Chromic Oxide Pigment in Subacute and Long-Term Feeding Experiment in Rats," (Ivankovic, S., Preussmann, R.; Food and Cosmetic Toxicology, 13:347-351, Pergamon Press, UK, 1975). **Experiment #1:** Chromic Oxide ( $\text{Cr}_2\text{O}_3$ , C-green 9, C-green 17,  $\text{CrIII}$ ) green cosmetic color, was fed in diet (bread) to BD rats at 0

(Altromin<sup>®</sup>), 2 (14M, 5F) and 5% (5M, 10F) for 90-days (5 days/week--toxicity). These rats were mated and all females were impregnated. Liver and spleen weights were decreased in both sexes at 2 and 5% Cr<sub>2</sub>O<sub>3</sub>. Treatment had no effect on fertility and there were no pup malformations, nor were there other toxic effects. **Experiment #2:** BD rats were fed Cr<sub>2</sub>O<sub>3</sub> in diet (bread) at 0 (Altromin<sup>®</sup>), 1, 2 and 5% for 2 years (60/sex/dose, 5 days/week [600 feeding days]--oncogenicity). No effects were observed which resulted from treatment (no oncogenicity). No histopathological changes occurred in any organ examined (limited number examined). No adverse effects indicated. These data are supplemental. (Kishiyama & Silva, 10/12/00).

012 132942 "Chromium and Chromium Compounds," (IARC Working Groups: 1972, 1979, 1982 and 1987 [IARC: 1973, 1979, 1980a, 1982, 1987a] in IARC Monograph Volume 49:49-256, 1990). The review includes exposure of workers (especially by inhalation), carcinogenic risk to metallic chromium, chromium[III] compounds and to chromium [VI] by multiple routes to experimental animals, reproductive effects and genotoxicity. In general CrVI has greater toxicity than CrIII. M. Silva, 11/29/00.

014 132948 "Chromic Acid Sixth Annual Report on Carcinogenesis," (Technical Resources for NIEHS, 1991, pages 48 - 53; submitted in book form, 461 pages total). This volume contains information on carcinogenicity, properties, exposure, use, production and regulations pertinent to various forms of chromium compounds. Certain chromium compounds mentioned in this review are considered to be carcinogenic. M. Silva, 11/29/00.

#### CONCLUSION:

There is sufficient evidence in humans for carcinogenicity of CrVI. Therefore the oncogenicity data gap is filled with an adverse effect for carcinogenicity of CrVI.

#### ONCOGENICITY, MOUSE

No study on file.

#### REPRODUCTION, RAT

No study on file.

#### TERATOLOGY, RAT

No study on file.

#### TERATOLOGY, Mouse

**\*\* 009 115199** "Developmental Toxicity Evaluation of Chromic Acid Administered by Gavage to CD-1 Mice," (Tyl, R.W., Marr, M.C., Myers, C.B.; Research Triangle Institute, NC; ID #: 60C- 4808-10/20; 11/12/91). Chromic Acid Solution -60% (purity = 55.05%) administered by gavage to mated CD-1 mice (25/dose) at 0 (deionized water), 5, 20, 60 or 120 mg/kg/day during gestation days 6 through 15. Maternal NOEL = 5 mg/kg/day (**Possible adverse effect: 1 dam at 120 mg/kg had total litter resorption.** Food

consumption was reduced up to 12, 19 and 28% for 20, 60 and 120 mg/kg/day, respectively. The death of a high dose dam was considered treatment-related.) Developmental NOEL = 20 mg/kg (There was an increased incidence in abnormalities (cleft palate, cleft sternum, perforated sternum) at  $\geq 60$  mg/kg). ACCEPTABLE. (Kishiyama & Silva, 9/25/00).

**001 045403** "Placental Transfer of Chromic Chloride and Its Teratogenic Potential in Embryonic Mice," (Matsumoto, N., Iijima, S., Katsunuma, H.; The Journal of Toxicological Sciences, 2(2)1-13, 1976). Chromic chloride was administered to mated ICR female mice, divided into 3 experiments: **#1:** Mice (9-11/dose) were injected at 0 (physiological saline), 9.76 and 19.52 mg/kg  $\text{CrCl}_3$  9 times subcutaneously every other day on gestation days (gd) 0-16, in order to measure CrIII retained by fetuses (placental transfer) and to examine effects on fetal growth. **#2:** On gd 7, 8 or 9, mice (5-7) received a single i.p. injection of 19.52 mg/kg  $\text{CrCl}_3$  to examine the teratogenic potential of CrIII on fetuses undergoing organogenesis. **#3:** Dams were injected with 9.76, 14.64, 19.52 and 24.4 mg/kg  $\text{CrCl}_3$  on gd 8 to test for a dose-response (7-13 pregnant mice). On gd 18, all pregnant mice were sacrificed and their uteri were examined for implantation and resorption sites. Fetal external and skeletal exams were also performed. **Results #1:** Maternal bodyweight gain was significantly decreased at  $\geq 9.76$  mg/kg. Cr concentrations were significantly increased in tissues at 19.52 mg/kg (gradient: spleen & kidneys > blood > placenta > fetus). **#2:** Fetal weights were significantly decreased. Embryonic and fetal death increased when dams were treated gd 8 (18.3%) and gd 9 (29.5%). External anomalies were significantly increased  $\geq$  gd 8 (exencephaly, open eyelids, cleft palate; skeletal defects in ribs & vertebrae). **#3:** Fetal weights were significantly decreased at  $\geq 19.52$  mg/kg. A dose-response (significant at > 14.64 mg/kg) for increased external anomalies: 26% open eyelid, cleft palate, exencephaly, acephalia and skeletal anomalies: 16.4%: rib fusion and cervical fusion occurred. **Possible adverse effects indicated (fetal developmental effects).** These data are supplemental. (Kishiyama & Silva, 10/18/00).

## TERATOLOGY, RABBIT

**009 115200** "Developmental Toxicity Evaluation of Chromic Acid Administered by Gavage to New Zealand White Rabbits," (Tyl, R.W., Marr, M.C., Myers, C.B.; Research Triangle Institute, Research Triangle Park, ID #: 60C-4808-30/40;12/13/91). Chromic Acid Solution -60% (purity = 55.05%) was administered by gavage to artificially inseminated female New Zealand white rabbits (16/dose) at 0 (deionized water), 0.1, 0.5, 2.0 and 5.0 mg/kg/day during gestation days 7 through 19. **Maternal NOEL** = 0.5 mg/kg (Mortality for does was 6.25 and 31% at 2 and 5 mg/kg/day, respectively. Abortion occurred in 8.33 and 33.3% at 2 and 5 mg/kg/day. The incidence of total litter resorptions (7-46%) was detected mainly as implantation loss. Food consumption was statistically significantly lower at 5 mg/kg/day but at 2 mg/kg it was decreased 12-21%. Clinical observations were increased at  $\geq 2$  mg/kg.) **Developmental NOEL** = 5.0 mg/kg (There were no treatment-related effects at any dose). UNACCEPTABLE. Too few pregnant does at scheduled sacrifice in all treatment groups. (Kishiyama & Silva, 10/3/00).

## GENE MUTATION

**011 132933** "Study of 106 Organic and Inorganic Compounds in the Salmonella/Microsome Test," (De Flora, S.; Carcinogenesis, 2(4)283-298, 1981). CrVI compounds: sodium dichromate, potassium chromate and chromic acid were tested using Salmonella typhimurium strains TA1535, TA1537, TA1538,

TA98 and TA100 (+/- S9 mix from Aroclor-induced rat livers). Two trials were performed (duplicate or triplicate plates/dose) at 50 to 250, 80 to 140 and 40 to 220 nmoles/plate, respectively to establish the range of activity and mutagenic potency for each compound. Results showed the mutagenic potency (#revertants/nmol) was 4.4, 2.9 and 5.1 for sodium dichromate, potassium chromate and chromic acid, respectively, when tested in Salmonella typhimurium strains TA1537, TA1538, TA98 and TA100. S9 mix decreased the mutagenicity of CrVI compounds. **Possible adverse effect indicated.** These data are supplemental. (Kishiyama & Silva, 10/19/00).

**001 045401** "Toxicity and Mutagenicity of Hexavalent Chromium on Salmonella typhimurium," (Petrilli, F.L., De Flora, S.; Applied and Environmental Microbiology, 33(4):805-809, 1977. Hexavalent chromium (sodium dichromate [Na<sub>2</sub>Cr<sub>2</sub>O<sub>7</sub>], calcium chromate [CaCrO<sub>4</sub>], potassium chromate [K<sub>2</sub>CrO<sub>4</sub>], chromic acid [CrO<sub>3</sub>]) at 10 to 800 ug/plate were used in a plate incorporation assay with Salmonella typhimurium tester strains TA1535, TA1537, TA98 and TA100 (+/-S9 Mix). In addition, a spot test was performed with 10 ul of each compound/spot (+/-S9 Mix). At 400-800 ug/plate (200-400 ug/ml) there was bacterial growth inhibition at all doses. There was a dose-response for increase in revertant colonies for all CrVI compounds at 10-200 ug/plate with TA1537, TA98 and TA100. Addition of S9 did not affect mutation incidence. CrIII compounds were also tested in this assay (chromium potassium sulfate & chromic chloride) but did not induce an increase in revertant colonies either with or without S9. Possible adverse effect indicated. These data are supplemental. (Kishiyama & Silva, 10/12/00).

SUMMARY: Although no adequate study has been submitted for genotoxicity, numerous positive reports are available demonstrating the genotoxicity of hexavalent chromium (see: - 012 132942 and - 011 132931).

## CHROMOSOME EFFECTS

**011 132932** "Mechanism of Chromium Toxicity in Mammalian Cell Cultures," (Bianchi, V., Dal Toso, R., Debetto, P., Levis, A. G., Luciani, S., Majone, F., Tamino, G.; Toxicology, 17 (1980) 219-224). Oxidized CrVI (chromic acid, potassium chromate, sodium chromate, potassium dichromate, sodium dichromate) and CrIII (Cr-chloride, Cr-nitrate, Cr-potassium sulfate, Cr-acetate) were tested on baby hamster kidney (BHK) and Chinese hamster ovary (CHO) cell lines for cytotoxic and cytogenetic effects. Results showed CrVI compounds had inhibiting doses (50%) at 100 – 375 times lower than those of CrIII compounds with BHK cells. LD<sub>50</sub> for CrVI compounds was more than 1250 fold lower than LD50 for CrIII with CHO cells. In CHO cells, there was a significant increase in SCE with CrVI compounds. CrVI at 0.25 to 1 ug/ml reduced cell growth by 300-fold and survival (as indicated by DNA and RNA synthesis) with BHK cells. The frequency of SCE (1.5 – 2.1-fold) and chromosome aberrations (3.3 – 9.9-fold) was increased in CHO cells when CrVI and CrIII (SCE = 1.0-1.1-fold; CA = 1.2 – 2.3-fold) compounds were used, when compared to controls. **Possible adverse effect indicated.** These data are supplemental. (Kishiyama & Silva, 10/18/00)

**001 045402** "Cytotoxic and Clastogenic Effects of Soluble Chromium Compounds on Mammalian Cell Cultures," (Levis, A.G., Majone, F.; British Journal of Cancer (1979) 40:523-533). Oxidized CrVI (chromic acid, potassium chromate, sodium chromate, potassium dichromate, sodium dichromate, calcium chromate) and CrIII (Cr-chloride, Cr-nitrate from 2 suppliers, Cr-potassium sulfate and Cr-acetate) were tested on Syrian hamster baby kidney fibroblast (BHK21) and Chinese hamster ovary (CHO) cell lines.

The tests assessed growth inhibition, cytotoxicity, sister chromatid exchange (SCE) and chromosomal aberrations. All CrVI compounds inhibited growth of BHK cells and decreased survival of CHO cells. Comparable effects occurred with CrIII, however only at 100-1000 times higher concentrations. Cytotoxicity curves for CrVI compounds were virtually overlapping, where marked differences were observed among CrIII compounds. Giant cells were obtained after exposure to both CrVI and CrIII compounds, as indicated by the increase in DNA and RNA content per cell (due to blocking cell cycle without inhibiting macromolecular synthesis). CrVI (0.5 - 2 ug/ml Cr<sup>+6</sup>) and CrIII (+150 ug/ml Cr<sup>+3</sup>) induce chromosome aberrations, while only CrVI induced SCEs (frequency was doubled). The frequency of chromosome aberrations was increased 10-fold with CrVI (1.0 ug/ml), but it is only doubled after treatment with up to 150 ug/ml CrIII. **Possible adverse effect indicated.** These data are supplemental. (Kishiyama & Silva, 10/13/00).

001 133308: Same study as 01 45402.

**001 045400** "Sister Chromatid Exchanges Induced in Cultured Mammalian Cells by Chromate," (MacRae, W.D., Whiting, R.F., Stich, H.F.; Chem.-Biol. Interactions, 26(1979) 281-286). Potassium chromate (K<sub>2</sub>CrO<sub>4</sub>) and potassium dichromate (K<sub>2</sub>Cr<sub>2</sub>O<sub>7</sub>) at 0 (Eagle's minimum essential medium + 15% Fetal Bovine Serum), 8 x 10<sup>-7</sup>, 1.2 x 10<sup>-6</sup>, 2 x 10<sup>-6</sup> and 3 x 10<sup>-6</sup> M and 10<sup>-8</sup>, 10<sup>-7</sup> and 10<sup>-6</sup> M were used on primary human fibroblasts (from a normal 24-year old female) over a 2h (acute) or 48h (chronic) treatment period to assess SCE's and for a 32h exposure to assess chromosomal aberrations. K<sub>2</sub>CrO<sub>4</sub> and CrCl<sub>3</sub> at 0, 10<sup>-7</sup>, 10<sup>-6</sup> and 10<sup>-5</sup> M were tested with CHO cells (24 & 32 h). N-methyl-N'-nitro-N-nitrosoguanidine (MNNG) was the positive control (10<sup>-7</sup>, 10<sup>-6</sup> & 10<sup>-5</sup> M), used with CHO cells only. After acute treatment (2h), cells were allowed to undergo 2 divisions in MEM + 5 uM BrdU. Chronic chromate treatment had cells in BrdU (5uM-lymphocytes; 20uM-CHO) harvested at various intervals up to 48 hours for assessment of SCE's. Prior to harvest, cells had to undergo 2 cell cycles (24h/cycle-fibroblasts; 12h/cycle-CHO). Results showed human fibroblasts had increased SCE's and chromosome aberrations (primarily breaks = 94%) at ≤ 10<sup>-6</sup> M. At 48 hours, both K<sub>2</sub>Cr<sub>2</sub>O<sub>7</sub> and K<sub>2</sub>CrO<sub>4</sub> induced a 4-fold increase in SCE in fibroblasts at 10<sup>-6</sup> M (at 2-hours, 1.5-fold increase at 10<sup>-6</sup> M). In CHO cells, CrCl<sub>3</sub> (CrIII) didn't induce increased SCE but both K<sub>2</sub>CrO<sub>4</sub> (CrVI) and MNNG (potent alkylating agent) induced SCE's over the same dose range (10<sup>-7</sup>-10<sup>-6</sup> M) but MNNG produced far more SCE's. Possible adverse effect indicated (increased SCE's and chromosome aberrations with K<sub>2</sub>CrO<sub>4</sub> and K<sub>2</sub>Cr<sub>2</sub>O<sub>7</sub>). These data are supplemental. (Kishiyama & Silva, 10/12/00).

**013 132947** "Increased Mutagenicity of Chromium Compounds by Nitrilotriacetic Acid," (Loprieno, N., Boncristiani, G., Venier, P., Montaldi, A., Majone, F., Bianchi, V., Paglialunga, S., Levis, A.G.; University of Pisa, Institute of Biochemistry, Biophysics and Genetics, Italy; 9/7/84; In: Environmental Mutagenesis 7:185-200 (1985)). Nitrilotriacetic acid trisodium salt (NTA), a substitute for polyphosphate in household laundry detergents and N-nitrosoiminodiacetic acid (NIDA) a derivative of NTA produced by metabolism of soil microorganisms were tested in vitro for mutagenicity with Salmonella typhimurium: TA1535, TA1537, TA1538, TA98 and TA100, Schizosaccharomyces pombe (P1) and Saccharomyces cerevisiae (D4) both with and without metabolic activation (S9). NTA (up to 40 ug/ml) and NIDA (up to 1000 ug/ml) were not mutagenic in these assays. NTA and NIDA were then tested in the sister chromatid exchange (SCE) assay in mammalian cell cultures (Chinese hamster ovary [CHO] cell line) along with water soluble chromium compounds (CrIII: Cr<sub>2</sub>[SO<sub>4</sub>]<sub>3</sub> & CrVI: Na<sub>2</sub>CrO<sub>4</sub>·4H<sub>2</sub>O and K<sub>2</sub>CrO<sub>7</sub>). The very insoluble CrVI

compounds ( $\text{PbCrO}_4$  &  $\text{PbCrO}_4\cdot\text{PbO}$ ) were mutagenic with TA100 in the presence of NTA or NaOH. Lead chromate mutagenicity was correlated with amount of CrVI solubilized by NTA or alkali. In the SCE assay, insoluble lead chromates were directly clastogenic due to prolonged exposure and cellular endocytosis. The chromosome-damaging activity of  $\text{PbCrO}_4$  was significantly increased by NTA but not by NaOH (0.5 N). **Possible adverse effect.** These data are supplemental. (Kishiyama & Silva, 10/10/00).

## DNA DAMAGE

**011 132932** “Mechanism of Chromium Toxicity in Mammalian Cell Cultures,” (Bianchi, V., Dal Toso, R., Debetto, P., Levis, A. G., Luciani, S., Majone, F., Tamino, G.; Toxicology, 17 (1980) 219-224). Oxidized CrVI (chromic acid, potassium chromate, sodium chromate, potassium dichromate, sodium dichromate) and CrIII (Cr-chloride, Cr-nitrate, Cr-potassium sulfate, Cr-acetate) were tested on baby hamster kidney (BHK) and Chinese hamster ovary (CHO) cell lines for cytotoxic and cytogenetic effects. Results showed CrVI compounds had inhibiting doses (50%) at 100 – 375 times lower than those of CrIII compounds with BHK cells.  $\text{LD}_{50}$  for CrVI compounds was more than 1250 fold lower than  $\text{LD}_{50}$  for CrIII with CHO cells. In CHO cells, there was a significant increase in SCE in CrVI compounds. CrVI at 0.25 to 1 mg/ml (limit of solubility) reduced cell growth by 300-fold and survival (as indicated by DNA and RNA synthesis) with BHK cells. The frequency of SCE (1.5 – 2.1-fold) and chromosome aberrations (3.3 – 9.9-fold) was increased in CHO cells when CrVI and CrIII (SCE = 1.0-1.1-fold; CA = 1.2 – 2.3-fold) compounds were used, when compared to controls. **Possible adverse effect indicated.** These data are supplemental. (Kishiyama & Silva, 10/18/00)

## NEUROTOXICITY

Not required at this time.

## ADDITIONAL INFORMATION

011 132931 “Chromium” (Agency for Toxic Substances and Disease Registry, US Public Health Service, in collaboration with the US Environmental Protection Agency, 7/89). This document contains a toxicological profile for chromium. Human data regarding exposure and carcinogenicity are also included (no worksheet). M. Silva, 11/30/00.

015 133218 “Epidemiological Evaluation of Koppers Company, Inc., Employee Deaths,” (Cote, R.W., Gregoire, A.T., Keller, M.D., Lanese, R.R., Williams, R.A.; Battelle, Columbus, OH; Department of Preventive Medicine, The Ohio State University, Columbus, OH; 12/3/73). This document was compiled to determine whether the employment environment is related to excess deaths due to any specific cause. This survey was an initial investigation which showed relatively few statistically significant differences among Divisions or between Koppers Company deaths and National data. Working for Koppers Company, Inc., was not associated with an increase in industrial risk (no worksheet). M. Silva, 11/30/00.



016 133719 “1978 Cross-Sectional Health Study of Workers at a Wood Preserving Plant,” (Tabershaw Occupational Medicine Associates, PA; Rockville, MD; 5/3/79). This document contains results of a cross-sectional health study performed on 63 of 74 “eligible employees.” Data showed no evidence of lung cancer or evidence of unacceptable systemic absorption of inorganic arsenic. The assessment of pulmonary (lung) system showed mild and moderate deficits in pulmonary function and atypical cells in cytologic examination of sputum. These findings were attributed to smoking. There was no evidence of liver or kidney disease or blood evidence of systemic abnormalities related to industrial exposure (no worksheet). M. Silva, 11/30/00.

017 133223 “Effects of Chemical Preservatives on the Health of Wood Treating Workers in Hawaii, 1981. Clinical and Chemical Profiles and Historical Prospective Study, July, 1983,” (Gilbert, Jr., F.I., Duncan, R.C., Lederer, W.H., Wilkinson, J.E.). This volume contains a study to evaluate morbidity and mortality of workers occupationally exposed to wood treating chemicals used in Hawaii for the years 1960 to 1981. The results showed no adverse health effects or increased incidence of mortality from exposure to wood preservative chemicals in the workers evaluated (no worksheet). M. Silva, 11/30/00.